EVOLUTION OF THE NERVE CELLS.

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THE work of His, who has succeeded in following in the embryos of mammals the different stages of development through which the ectodermic elements pass in order to transform themselves into nerve cells, have brought some important explanations to the interesting question of the evolution of the nerves cells.

Lachi, Cajal, Lenhossek and Retzius have confirmed the results obtained by His, and have continued this kind of research.

We will give here an abstract of this subject by utilizing the most recent data.

The epithelia of the medullary furrow of the ectoderm (medullary plate) contains two kinds of elements; some long epithelial cells reaching from one surface of the membrane to the other, and some spherical cells, situated near the external face of this same membrane, which is grooved inward. These last corpuscles, called germinal cells, give origin by an active karyokinesis to the neuroblasts, or rudimentary nerve cells. The epithelia produces the cells of the ependyma and those of the neuroglia exclusively.

GERMINAL CELLS AND NEUROBLASTS, AND THE DEVELOPMENT OF THE AXIS CYLINDER.

When the medullary furrow has closd in order to form the medullary tube, the inner surface of the embryonic marrow is thickened, and at the same time an important differentiation is produced in its cells.

Many of the germinal cells emigrate toward the peripheral half of the medullary wall. During their journey they are transformed into neuroblasts; that is to say, into pyriform cells presenting an ovoid body directed either behind or within, and having only one relatively large expansion (process) which is extended lengthwise and passes toward the periphery, through the rudimentary gray substance. This primordial extension is the axis cylinder.

In preparations stained with carmine or hematoxylin, it is not possible to see the extremity of the axis cylinder in the course of its development; consequently His was not able to distinguish it in a very clear manner, and was therefore not prepared to successfully answer Hansen, who denied the growth of the nerve fibres toward the periphery; for, said he, no investigator has yet seen the end of the axis cylinder in the course of its development.

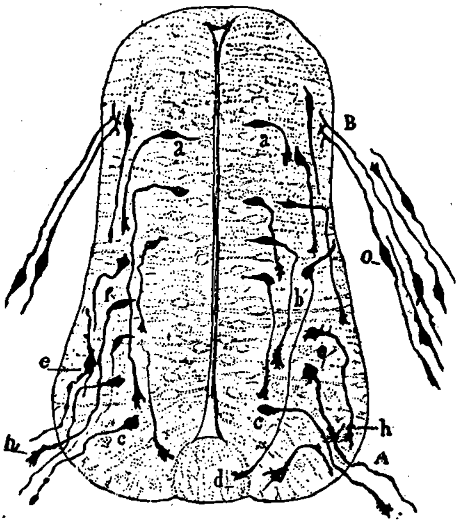

FIG. 1. Section of the spinal cord of a chick in the third day of incubation.

A. Anterior root; B. Posterior root; a. Very young neuroblasts; b. Other neoroblasts, more developed and probably commissural; c. Neuroblasts of the anterior roots; d. Cone of growth of a commissural axis cylinder, h. and i. Cones of growth of anterior roots; e. Radicular cells which already present rudiments of protoplasmic branches; o. Ganglionary cells.

Our observations made on the spinal cord of a chick in the third day of incubation, have enabled us to solve definitely this problem and to pronounce ourselves in favor of

His and against the theory of Hansen. We have demonstrated that every primordial axis cylinder, while extending through the marrow, terminates by a special conic enlargement (*cone of growth,*) the base of which, directed toward the side of the periphery, is furnished with numerous asperities and lamellary expansions which we may consider as rudimentary terminal arborizations. This cone of growth is like an amæboid mass, which, acting in the manner of a battering-ram, scatters the elements that are in its way and insinuates its lamellary expansions among them. Fig. 2 illustrates the neuroblasts as they appear in the spinal cord of a chick from the third or fourth day of incubation. There is seen also lying in the anterior region of the marrow, a group of cells which send their cones of growth to the anterior root; another group of neuroblasts disseminated through almost the entire gray substance, but accumulated more particularly in the most posterior region, directs its cones of growth toward the anterior commissure. Finally a small number of neuroblasts insinuate their nervous expansions in the peripheral region of the cord, the future territories of the white columns. Here these expansions form an elbow or divide themselves into a T, as the case may be, in order always to take a vertical direction. While such metamorphosis are taking place in the germinal cells the epithelium do not remain inactive.

EPITHELIUM CELLS AND THE FORMATION OF NEUROGLIA.

Every epithelial cell may be considered as made up of two parts; one part external and the other internal. The internal part is almost smooth, and, containing the nucleus, is separated from the expansions of the neighboring epithelium by some long spaces where are lodged a large number of neuroblasts (layer of the column of His); the external part is furnished with multiple short collateral expansions resembling thorns. These place themselves in contact with those that come from neighboring epithelial cells and thereby form a woof of spongy appearance, whose interstices will serve as a means of passage for the nerve fibres of the white substance (Marginal veil or Randschleier of His). According to His, these interstices are formed before the nerve fibres. Their role would therefore be very important, for they would then represent a kind of pre-estab-

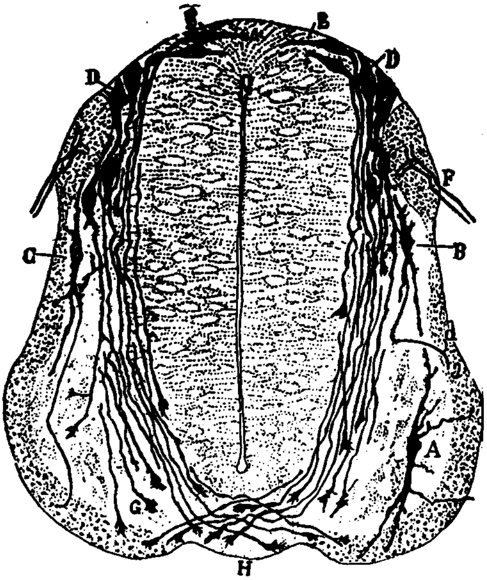

FIG. 2. Section of the dorsal marrow of an embryo of a chick in the fourth day of incubation.

A. Cell of the anterior root; B Cell of the antero-lateral column; C. Cell of the anterior column; D. Pyriform neuroblasts whose axis cylinder terminates at the level of the anterior commissure by a cone of growth; E. Nervous primordial cells which still preserve the form of the spongioblasts; F. Posterior root; G. Cones of growth; H. Embryonic anterior commissure.

lished, conducting canals through which the extremities of the axis cylinders would be obliged to pass. It appears to us, however, that the expansions of the epithelial cells, and consequently that the interstitial spaces of the marginal veil of *His*, are not formed before, but rather after the peripheral fibrillary substance; we have seen in addition to this that in the retina and the brain all the most important differentiations of the nerve cells, the growth and distribution of the axis cylinders, take place at a time when the epithelial cells are still reduced to a state of simple radiating fibres deprived of all lateral expansions.

However it may be, we must consider the theory of His, who claims that the growth of the nervous fibres is always in the direction of the least resistance, and that their direction is determined by the pre-existence of the

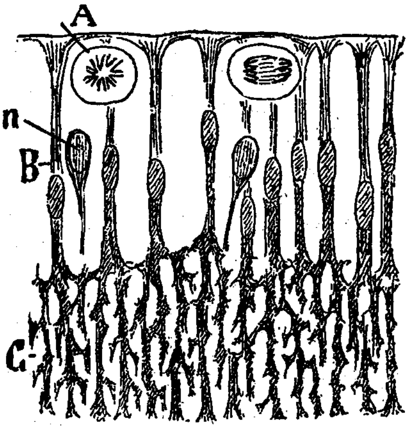

FIG 3. Section of the embryonic spinal cord.
A. Germinal cells; B. Internal portion of the epthelial cells (layer of the pillars); C. External portion of the epthelial cells (reticular layers or marginal veil); N. Neuroblast (after His).

formation of neuroglia, as an ingenuous hypothesis and one worthy of study.

Perhaps it would be preferable to conceive in the neuroblasts a sort of positive *chemiotaxis* created by some nutritive substance elaborated in some other elements, either nervous, epithelial or muscular. One could also explain the power which incites the neuroblast to send its nervous prolongation toward a muscle, for instance by the existence of two electric states, different in the neuroblasts and in the muscle. This is the hypothesis recently brought forward by Strasser. Under the influence of a state electro-negative of the muscular fibre or any other cell which received the terminal arborizations of the nervous prolongation, there would be produced in the external pole of the neuroblast an electro-positive condition, which would induce it to work in the direction of the greatest difference of potential.

DEVELOPMENT OF THE PROTOPLASMIC EXPANSIONS AND OF THE COLLATERALS.

It is by the rapid method of Golgi that the last phases of development of the neuroblasts have been fully studied. The observations made on the spinal cord of the chick by Lenhossek and us, independent one from the other, have completed the cycle of the works of His in showing in what way and at what time the protoplasmic arborizations and the collaterals of the nerve processes take their birth.

As soon as the axis cylinder is formed there may be seen on the neuroblast a short polar expansion, which might be considered as the beginning of a protoplasmic prolongation. Nevertheless this polar expansion is often absent, and the protoplasmic expansion usually commence by presenting themselves under the form of large excrescences of a thorny aspect, starting either from any point of the neuroblastic body or from the origin itself of the axis cylinder. Their free extremity is often provided with a varicosity.

The collaterals of the nerve process originate in their turn a few days after the formation of the protoplasmic expansions. They begin by a short appendix, departing at a right angle and terminating by means of a varicosity. The collaterals which appear first in the cord are those of the anterior column (from the fourth to the fifth day of incubation in the chick). In the following days one sees the beginning of the collaterals of the posterior and lateral columns. As to the bifurcations of the axis cylinders (fibres in the T or Y), we have already said that they begin to form during the period of growth of the primitive nerve expansion.

It is very easy to perceive the growth from life in the spinal cord of a chick from the fifth to the seventeenth day of incubation; that is to say, the march of the nerve fibre of the anterior root toward the muscles. Generally, the anterior root is completely formed by the fifth day, and its fibres have made such development that it is impossible to find their extremities within the limits of the anterior root. They are already found engaged in the neighboring muscular masses under the form of varicosities. Every axis cylinder during its journey gives off an extraordinary number of ramifications; thus in the embryo of a chick seventeen days old we have seen a large motor fibre producing more than thirty terminal branches, each one destined to a muscular fibre. The motor plates which are not yet formed are represented by a varicose fibre terminated by a small sphere placed on the muscular cell. In some plates the nerve fibre began to produce a certain number of short

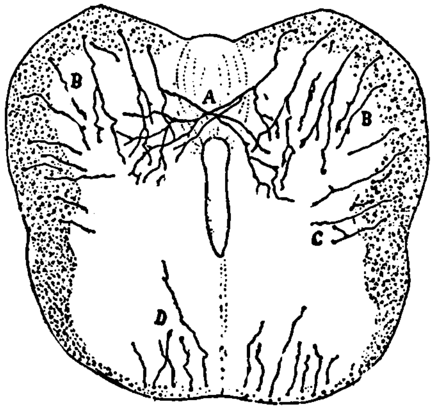

FIG. 4. Section of the marrow of the embryo of the chick of the seventh day of incubation.

A. Collateral fibrils of the anterior column, forming a crossing in the anterior commissure; B. Collateral fibrils, less developed, terminated by cones of growth; C. The youngest of the collaterals belonging to the lateral column; D. Collaterals of the posterior column.

excrescences, the first rudiments of the terminal arborization.

The preceding description is applicable to most nerve cells; however, there are a few which behave in a different manner and possess in their evolution peculiarities which may be expressed in a few words.

CELLS OF THE SPINAL GANGLIA.

In mammals, birds, bactrachia and reptiles the nerve cells of the spinal ganglia are unipolar. It is only in fishes that one finds them in the bipolar form, similar to the olfactory cells of the nasal chambers, or to the cells of the spinal ganglion of the snail.

There seems to be an essential difference relative to the morphology of the ganglionic sensory cells in the higher vertebrates and fishes. But His has discovered a fact of the greatest interest. It is the following: the corpuscles of the sensory ganglia are bipolar in the embryos of mammals entirely the same as in adult fishes. This diminishes the distance that used to appear to separate them.

Of the two primitive expansions, the internal, generally more slender, grows along the posterior root and penetrates into the posterior column of the spinal cord, where, as our observations have been able to establish, it bifurcates in order to form an ascending and descending branch; we have been able to discover on this branch of these cells in the embryo of the chick of three days, a cone of growth directed toward the spinal cord; the external branch grows toward the periphery. It mixes with the motor fibres in the spinal nervè trunk and terminates finally in the skin, in the mucous membrane or in the musculo-tendonus organs of Golgi.

The bipolar cells undergo some modification during the growth of the spinal ganglia.

As has been very well figured by His, whose observations have been confirmed by us,on the embryos of some birds and reptiles, and also by Lenhossek, C. Sala, Retzius, E. Müller, Van Gehuchten, the extremities of protoplasm, which give root to two expansions, draw nearer one another, unite with each other gradually, and form on one side of the cell a pedicle of protoplasm, the only support for the two nerve fibres.

Fig. 5, which represents a spinal ganglion of the embryo of a chick on the fourteenth day of incubation, shows very distinctly all the transitions between the bipolar and unipolar phases. On examining this figure one receives the impression of a general emigration of the cellular corpuscles toward the periphery of the ganglion, the centre remaining reserved for the nerve fibres and the pedicle of bifurcation. These facts are then the proof that in the cellular ontogeny of the vertebrates there exist some evolutive transient phases which remain permanent in the fishes.

This is not all. Lenhossek has again demonstrated in certain fishes (embryos of the Pristurus) the presence of unipolar elements near the bipolar cells. It is thus seen that the transition from bipolarity into unipolarity begin in certain adult fishes.

It results from all these works that every sensory or sensorial cell is a bipolar corpuscle, or has been so in the embryonic epoch. All sensory or sensorial cells are always provided with two expansions: one peripheral, destined to receive the centripetal excitations produced at the surface of the body, and the other central, its office being to conduct to a nerve centre the excitations received by the first. Considered in this manner, the

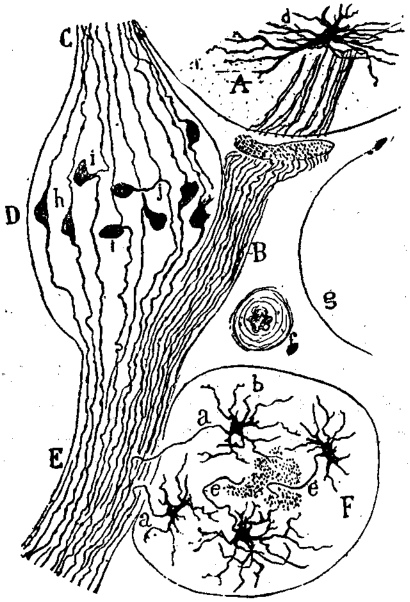

FIG. 5. Sympathetic and spinal ganglia of the cervical region of the embryo of a chick at the seventeenth day of incubation.

A. Spinal cord where is seen a radicular cell, d ; B. Anterior or motor root; C. Posterior or sensory root; D. Spinal ganglion ; E. Cervical spinal nerve ; F. Sympathetic ganglion ; a. Sympathetic axis cylinder forming the communicating rami and directed toward the corresponding spinal nerve ; b. Protoplasmic expansion of the sympathetic cells; e. Sympathetic axis cylinders becoming vertical to form the longitudinal commissure of the ganglia ; h. Fusiform cell of the spinal ganglion ; i. Transition of the bipolar cell into the unipolar cell of the spinal ganglion ; j. A distinctively unipolar cell ; f. Artery cut across ; g. Body of cervical vertebra.

sensory and sensorial cells form a well-defined variety, in which are naturally included :

(1) The cells of the spinal ganglia.

(2) The bipolar cells of the olfactory mucous membrane.

(3) The bipolar cells of the retina and the bipolar cells of the organ of hearing.

To this category belong also the fusiform corpuscles, discovered a short time ago by Von Lenhossek in the skin of the lumbricus, and whose existence has been confirmed by Retzius. These cells possess a large peripheral expansion terminating at the surface of the epidermis, and a fine central expansion, which, penetrating into the interior of the body of the animal, goes to the ganglionary chain, where, like the fibres of the sensory root of the vertebrates, it bifurcates into an ascending and a descending branch. These singular corpuscles would represent, therefore, the cells of the spinal ganglia of the vertebrates, with the only difference that in worms, the protoplasmic mass of the cellular body (product of the ectodermic layer) has not retired into the interior of the body in order to form the ganglionary masses.

CELLS WITH PROTOPLASMIC TUFTS.

The cells of Purkinje of the cerebellum, the pyramidal cells of the brain, the ganglionary cells of the retina, pass also through the phase of the neuroblast. But the development of their protoplasmic expansions is made in a particular way and in an order which is important to know. That which appears at first after the axis cylinder is ordinarily the peripheral tuft, at first irregular and extremely varicose; later the protoplasmic peripheral boquet moves away from the cell, and thus is formed the vertical stem. The collateral branches of the stem and the basilar branches of the cellular body are always formed last. In the pyramidal cells of brain these basilar expansions persist and take even a large development. This is not the case with the cells of Purkinje and the ganglionary cells of the retina, where they appear almost at the same time with the expansion or principal stem. Here they are atrophied and disappear totally.

GRANULES OF THE CEREBELLUM.

The cells pass through extremely peculiar metamorphoses, which recall in part those of the unipolar corpuscles of the spinal ganglia. The cerebellum of newborn mammals,—mouse, rabbit, dog, man, etc.,—possesses, as we know, above the molecular layer, a special zone formed by small corpuscles piled one against another, which are called superficial granules. But these corpuscles diminish in number in proportion as the cerebellum advances in its evolution; and there comes a time at maturity when they disappear completely. What is then the destiny of those cells whose number diminishes precisely in proportion as those of the true granules develop? At the beginning of our study on the cerebellum we have already observed that the deep layers of the superficial granules are composed of long fusiform bipolar cells, extended horizontally and provided with long expansions of a nervous appearance, all directed parallel to the longitudinal axis of the lamellar cerebellus. It would have been thought that it was a question of parallel fibres similar to those which grow from the axis cylinder of the deep granules. Well, these bipolar cells are not in reality anything else but the primitive forms of the deep granules. By means of an emigration across the molecular layer subjacent, these corpuscles, contrary to the bipolar cells of the spinal ganglia, which from central become peripheral, take the direction of the lamellar of the cerebellum to assume there, all the characters of the adult granules. Before attaining that, these corpuscles pass through the following changes:

(1) From the body of the horizontal bipolar cell descends a protoplasmic appendix, which, little by little, carries backward the cellular body including the nucleus.

(2) This appendix which advances perpendicularly in the thickness of the molecular zone forms there an extended element, provided with two expansions, the ascending one extending itself to the superior part of the molecular layer by a parallel fibril; the descending one finishing freely near the zone of deep granules.

(3) When the cell carried away, so to speak, by and in the descending appendix, has reached the layer of the deep granules, one sees the ascending expansion becoming thinner and taking the appearance of an axis cylinder, which is continued by a parallel fibril; then the cellular body gives birth to three or several short appendices which do not take long in becoming the characteristic protoplasmic expansions of the deep granules.

This evolutive history, then, teaches us two interesting facts:

First, we see the parallel fibril fasten itself, so to speak, as a fixture and in a definite manner in the region which it occupied when at first it was represented by two extremities of the horizontal bipolar cell; this is exactly what we saw produced in the spinal ganglia; afterwards it is the ascending axis cylinder and the digitiform expansions of the granule that are found to be the result of a protoplasmic expansion.

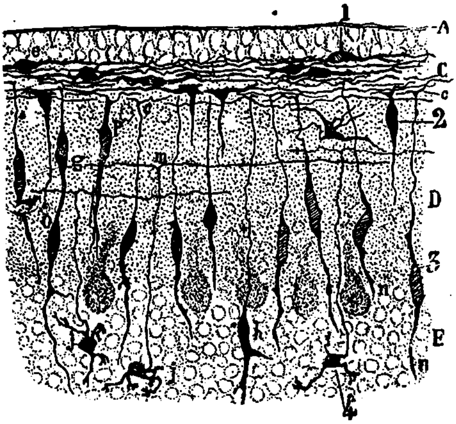

FIG. 6. Section of the cerebellum of a twelve-day-old mouse, wherein is seen the evolution of the granules.

A. Layer of the superficial granules; C. Layer of the horizontal bipolars; D. Molecular layer; E. Layer of the vertical or deep granules; first phase of the granule (horizontal bipolar cell); second phase of the granule (vertical bipolar by the production of the descending appendix which becomes the cellular body); third phase of the granule (the ascending axis cylinder is very perceptible and the inferior extremity of the cell already extends to the layer of the deep granules); fourth phase of the granule (completely developed granule).

SPONGIOBLASTS OF THE RETINA.

The nervous corpuscles which lack axis cylinder do not pass through the neuroblastic phase. Such is the case with the non nervous spongioblasts of the retina; that is to say, those which are not provided with an axis cylinder. In them the cellular body emits first through its inferior side a large boquet of short varicose fibrils. This is nothing else than the first appearance of the terminal arborization. Later on the body extends itself in a vertical direction, and its inferior extremity is transformed into a stem to which is suspended the terminal arborization. Such is at least the evolution of a few spongioblasts of the retina in the chick and the rabbit.

The non-nervous spongioblasts of the retina are not the only elements existing with these evolutive and morphological characters in the animal series. They are, as to their form, abundantly represented, and may be considered as a type of the phase of the morphological evolution to which come, for example, the cells of the invertebrates. Thus, according to the works of Bierdermann, Retzius and Lenhossek, the nerve cells of the ganglia in invertebrates (crustaceans and worms) are for the most part of unipolar form. Their unique expansion, in general very thick, furnishes then freely finished collaterals to the interior of the ganglia. When the cell is multipolar, all the expansions seem to have the same character; that is to say, they may all be considered as of a functional nature (Retzius). In the vertebrates the central cells on the contrary have experienced unimportant transformations which have brought them a long distance from the primitive neuroblastic form, so frequent in the centres of adult invertebrates. Some primitive forms, however, persist still, which have not suffered any differentiation in their expansions and resemble more or less neuroblasts. They are the spongioblasts of the retina, as we have just seen. The granules of the olfactive bulb. The sympathetic visceral cells and intestinal cells (plexus of Auerbach, of Meissner, etc.), and probably also certain cells of the cerebral cortex.

Vomiting of Nervous Origin.—Ulinski (*Die Therapie der Gegenwart*, March, 1895), treated two hysterical patients for nervous vomiting according to the method of Winternitz. One was a case of gastric hyperæsthesia and the other was associated with genital reflex. The patients bodies were enveloped in a damp, cold sheet, upon which, over the region of the stomach, a coil of rubber tubing was placed. One end of the tube was conducted to a vessel on the floor and the other end led to another vessel filled with water at 40° R. and placed above the patient in such a manner that a running stream circulated through the coil of tubing. The patients were then wrapped in a dry sheet. The applications were made half an hour before administering food. The object of this procedure is to diminish the sensibility of the nerves of the gastric mucous membrane and thus cause cessation of the vomiting. Ulinski believes that the rubber coil exerts a direct sedative influence on the gastric nerves. FREEMAN.